SOCIO – CLINICAL, BIOCHEMICAL AND ELECTROCARDIOGRAPHIC ASPECTS OF YELLOW OLEANDER POISONING

Dissertation submitted for

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CERTIFICATE

This is to certify that this dissertation titled *"**SOCIO – CLINICAL, BIOCHEMICAL AND ELECTROCARDIOGRAPHIC ASPECTS OF YELLOW OLEANDER POISONING"*** submitted by **Dr. Vimal Abraham** to the faculty of General Medicine, The Tamilnadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD degree Branch I (General Medicine) is a bonafide research work carried out by him under our direct supervision and guidance.

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DECLARATION

I, **Dr. Vimal Abraham,** solemnly declare that the dissertation titled "***SOCIO–CLINICAL, BIOCHEMICAL AND ELECTROCARDIOGRAPHIC ASPECTS OF YELLOW OLEANDER POISONING"*** has been prepared by me.

This is submitted to the Tamil Nadu Dr.M.G.R. Medical University, Chennai, in partial fulfillment of the regulations for the award of MD Degree Branch I (General Medicine).

It was not submitted to the award of any degree / diploma to any university either in part or in full form previously.

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CONTENTS

INTRODUCTION

The yellow oleander (Thevetia peruviana) is an ornamental tree of the Apocyanaceae family that is widely distributed throughout the tropical to the subtemperate zones of the world. Their beautiful yellow flowers and prolific growth makes them popular shrubs for landscaping. These plants also may be found growing wild[1].

All parts of the plant contain cardiac glycosides. The major toxic effects are similar to that of digoxin overdose. The pathophysiology includes direct glycoside inhibition of sodium-potassium pump of the heart and increased vagotonia. Symptoms include vomiting, diarrhea, dizziness, bradycardia, sinus and AV nodal block and other cardiac dysrhythmias[2,3]. Fatal, DC shock resistant ventricular fibrillation or refractory cardiogenic shock may occur in severely poisoned patients[4] .

Accidental ingestion occurs in children due to beautiful yellow flowers and the conspicuous green fruit[5]. Accidental poisonings have been reported form across the world, for example the Solomon Islands, Brazil and Australia. However, intentional poisoning in these regions is very uncommon[6]. But the use of seeds / fruits of yellow oleander as a method of suicide is common only

in Srilanka and South India. Following the death of two girls in 1980 which was widely reported in newspapers there has been a sudden increase in the number of cases of suicidal yellow oleander poisoning in Srilanka with thousands of cases occurring each year now with a case fatality rate of at least 10%[4].

Though the poisoning is a common method of suicide in South India there has been no published reports regarding this poisoning from South India. Data regarding incidence and case fatality rate of this poisoning in South Indian population is not available. The only Indian study involving large number of patients is from Eastern India. (300 cases, Bose TK et al, 1999).[7] Although clinical, biochemical and electrocardiographic characteristics of yellow oleander poisoning have been previously reported, social profile of patients has not been well studied. Hyperkalemia which has been noted in about 30% of the cases of yellow oleander poisoning in a Srilankan study has not been described in Indian studies involving 300 patients and 32 patients respectively.[7,8] The risk factors for cardiotoxicity and outcome have also not been studied in detail in previous studies. Moreover further studies are required to support the use of multiple doses of activated charcoal and anti-digoxin Fab fragments in yellow oleander poisoning. There has been only one clinical trial each to support their use in yellow oleander poisoning.[9,10]

So this study was undertaken to find out the incidence of yellow oleander poisoning among admissions in general medicine wards of our hospital, to study the socio-clinical aspects, to find out correlation between clinical and biochemical parameters with electrocardiographic changes and to assess possible risk factors for cardiotoxicity and outcome and to compare the results with previous published reports.

REVIEW OF LITERATURE

Yellow Oleander (Thevetia peruviana) - Plant description and distribution

It is a small ornamental tree belonging to family Apocynaceae which grows to about 10 to 15 feet high. The leaves are spirally arranged, linear, lanceolate and about 13 to 15cm in length. Flowers are bright yellow and funnel shaped with 5 petals spirally twisted. The fruits are somewhat globular, slightly fleshy and have a diameter of 4 to 5cm. The fruits which are green in colour, become black on ripening. Each fruit contains a single nut, light brown in colour and triangular in shape with two cells, each enclosing a pale yellow seed.[5]

These plants are widely distributed throughout the tropical to the sub-temperate zones of the world. Their beautiful yellow flowers and prolific growth makes them popular shrubs for landscaping. These plants also may be found growing wild[1]. It is often planted in numbers as a hedge[11].

Historical and Medicolegal aspects

Many myths are associated with this plant. In the West Indies, the nut is carried in the pocket in the belief that it will ward off hemorrhoids. In East Africa, it is put in the hand of an infant at birth as a good luck token. In

Africa, the seed kernels are occasionally chewed to cause purging. In the Philippines, half of one leaf in given as emetic and purgative. The sap and bark have been utilized in small amounts to treat malarial fever as well as to induce vomiting and purging. The sap also has been applied to sores and ulcers, also to tooth cavities and decayed teeth to relieve toothache[11].

The toxicity of the plant has been generally known since the sixteenth century. It's Sankrit name "Ashwamarak" is translated as horse killer[11]. Accidental poisoning occurs in children as they may play with and taste the bright yellow flowers and conspicuous green fruit. The seeds are used for suicide attempts particularly by young people especially in northern parts of Srilanka and South India. Other medicolegal aspects include use of roots and seeds with water or oil for procuring criminal abortion and seeds for poisoning cattle.[5] Yellow oleander glycosides proved effective in patients with heart failure and atrial fibrillation in studies carried out in 1930s, however digoxin has been preferred because of less frequent gastrointestinal side effects.[12]

Epidemiology of yellow oleander poisoning

Ingestion of oleander seeds or leaves is a cause of accidental poisoning worldwide, particularly among children.[6,13] Cases have been reported from places as diverse as Hawaii, the Solomon Islands, Southern Africa, Australia, Europe, the Far East and the United States.[14,15] However the use of seeds / fruits of yellow oleander as a method of suicide is common only in Srilanka

and South India. This method of suicide is common among adolescents and young adults with a female preponderance[4,7]. Currently, thousands of cases of yellow oleander poisoning occur in Srilanka every year with a case fatality rate of atleast 10%.[4] The exact incidence of the disease in Indian population is not known. Bose TK et al (1999) noted a case fatality rate of 4.6% among 300 cases in Eastern India.[7]

Poisonous parts

All parts of the plant are poisonous especially the seeds / kernels of fruit.[16]

Poisonous agents

Thevetin A & B, Thevetoxin, Peruvoside, Ruvoside and Neriforin which are cardiac glycosides are the poisonous agents found in this plant[17].

Pathophysiology of toxicity

The poisonous agents found in yellow oleander plant are cardiac glycosides. These bind to a site on the cell membrane, producing reversible inhibition of sodium (Na^+) – potassium (K^+) – adenosinetriphosphatase (ATPase) pump, which causes increased intracellular sodium and decreased intracellular potassium. In myocytes, elevated intracellular sodium concentrations produce increased intracellular calcium concentrations via a

sodium (Na^+)- calcium (Ca^{2+}) exchanger. Excessive intracellular calcium is concentrated in the sarcoplasmic reticulum and released in excess, with depolarization.[18]

Release of excessive calcium results in enhanced cardiac contractions which are delayed after depolarizations and manifest clinically as after contractions, such as premature ventricular contractions. Cardiac glycosides also have vagotonic effects, resulting in bradycardia and heart blocks. Inhibition of Na^+-K^+-ATPase in skeletal muscle results in increased extracellular potassium and contributes to hyperkalaemia[18]. Severe hyperkalemia can contribute to atrioventricular (AV) block and depressed myocardial excitability.[19]

Cardiac glycosides primarily affect cardiovascular and gastrointestinal systems of which effects on the cardiac system are most significant. The pathophysiology that produces cardiotoxicity involves prolonging refractory period in the atrioventricular (AV) node, shortening refractory periods in the atria and ventricles, and decreasing resting membrane potential (increased excitability). Any dysrhythmia characterized by both increased automaticity and depressed conduction is suggestive of cardiac glycoside toxicity.[18]

Dysrhythmias often associated with cardiac glycoside toxicity include bradydysrhythmias, sinus bradycardia with all types of atrioventricular (AV) nodal block, junctional rhythms and sinus arrest. Dysrhythmias characterized

by increased automaticity and conduction blockade, are highly suggestive of cardiac glycoside toxicity. These include tachydysrhythmias such as atrial tachycardia with block, paroxysmal atrialtachycardia with block, bidirectional ventricular tachycardia and ventricular fibrillation[18].

Pharmacokinetics

Thevetin is easily absorbed from the gastrointestinal tract. Thevetin glycosides occur in higher concentrations in heart muscle than in blood.[20] Thevetin probably has a shorter half-life than digoxin and a lower risk of accumulation in the body[17].

Fatal dose

Although previous authors have suggested that between four and seven seeds was the lethal dose[2,3], recent studies in Srilanka involving larger number of patients found that there was no exact relationship between number of seeds ingested and outcome.[4]

Clinical features of yellow oleander poisoning

Symptoms

Closely resembles digitalis poisoning with gastrointestinal and cardiac symptoms.

Gastrointestinal symptoms

Symptoms are nonspecific and include nausea, vomiting, diarrhea and abdominal pain.[2,3]

Cardiac symptoms

Include palpitations, shortness of breath, giddiness etc.[18]

Neurological symptoms

Pupils may be dilated.[21] and excessive salivation has been reported.[20] Paraesthesias and weakness have also been reported.[20] Symptoms are often nonspecific and include giddiness, numbness (especially of tongue and oral mucous membranes), altered mental status (eg. Disorientation, confusion, drowsiness, lethargy etc.) and occasionally seizures. [18]

Complications

1. **Cardiogenic shock** can develop secondary due to arrhythmias. The various arrhythmias that are noted in yellow oleander poisoning are sinus bradycardia, sino-atrial block, all types of atrioventricular (AV) block including Mobitz type II second degree AV block, junctional rhythm, supraventricular tachycardia, atrial fibrillation, artrial flutter, bundle branch block, ventricular ectopics, ventricular tachycardia and ventricular fibrillation.[8]
2. **Hyperkalemia** is seen in severe cases of yellow oleander poisoning[8].

3. **Acute renal failure** can develop secondary to cardiogenic shock.
4. **Acid base disturbance-**circulatory collapse can cause metabolic acidosis.

Postmortem appearance

Subendocardial and perivascular hemorrhage with focal myocardial edema has been noted.[7] Generalised hemorrhages and signs of gastrointestinal irritation have also been found.[5]

Course and prognosis

In severe poisoning diarrhea, vomiting, abdominal pain and sinus bradycardia are early features. Hyperkalemia, conduction block and ventricular ectopics indicate serious toxicity .[20] Indicators of a poor prognosis include multiple and varying cardiac rhythms, with sino-atrial and atrio-ventricular blocks in combination with ventricular excitability, ST depression over 2.5mm and unresponsiveness to atropine.[2] Conduction block and sinus bradycardia may persist for 5 days after ingestion. Patients usually recover from these if no underlying cardiovascular pathology exist [20].

Management

Investigations

Blood glucose estimation: assess for hypoglycemia as a possible cause of altered mental status.

Electrolytes

Hyperkalemia occurs in severe yellow oleander poisoning. The degree of hyperkalemia correlated with the serum digoxin cross reactive cardiac glycoside concentration[8]. Severe hyperkalemia can contribute to atrio-ventricular (AV) block and depressed myocardial excitability[19]. Hypokalemia can also exacerbate cardiac glycoside toxicity due to enhanced binding of cardiac glycoside to Na^+-K^+ ATPase pump[22]. Electrolytes has to be checked repeatedly, particularly serum potassium levels. Hypercalcemia and hypomagnesmia also can exacerbate cardiac glycoside toxicity.

Blood urea and creatinine

Acute renal failure can develop secondary to cardiogenic shock. Renal insufficiency is associated with elevated endogenous digoxin like immunoreactive factors that can give false – positive digoxin assay results[18]. Renal function has to be closely monitored.

Cardiac glycoside level

Some plant glycosides cross react with commonly used digoxin radioimmunoassay and digoxin fluorescence polarization immunoassays[23]. Detectable levels of cardiac glycosides have been associated with ingestion of foxglove and oleander however levels do not correlate with severity of illness. Beyond its qualitative usefulness in oleander toxicity, however the digoxin serum levels clinical significance is unknown. Negative digoxin

radioimmunoassay does not rule out a plant glycoside exposure[18]. In one of the Srilankan studies there was a correlation between degree of hyperkalemia and the serum digoxin cross reactive cardiac glycoside concentration. But they could not identify cardiac glycoside levels or hyperkalemia at presentation as determinants of mortality[8].

Electrocardiogram (ECG) and continuous cardiac monitoring

To find out the cardiac rhythm, identify life threatening arrhythmias and for treatment.

Hemoglobin level - To determine if anemia is a cause or potential complicating factor for dysrhythmia or hypotension.

Arterial blood gas analysis – To identify metabolic acidosis which may develop secondary to circulatory collapse.

Sample collection – Remaining parts of the ingested plant and gastric contents are useful for botanical identification. Plant portions found in vomitus should be stored in a plastic bag for forensic examination.

Treatment

General principles include providing general supportive care, immediate gastric decontamination, preventing further exposure and absorption, administering antidote and correction of arrhythmias and

electrolyte disturbance. Management is very similar to that of digoxin poisoning.

Decontamination

If consciousness is not impaired, emesis can be induced or gastric lavage can be performed. Gastric lavage is most useful when started within sixty minutes after ingestion[24].

Activated charcoal

Activated charcoal can be given 60-100g orally or via gastric tube, mixed in aqueous slurry[24]. Multiple doses of activated charcoal (50 g of activated charcoal every 6 hrs for 3 days) has been found to be more effective in reducing deaths and life-threatening cardiac arrhythmias after yellow oleander poisoning than single dose. After absorption into the systemic circulation cardiac glycosides are secreted into the gut lumen by the action of p-glycoprotein (enterohepatic circulation). In gut, activated charcoal binds the secreted glycoside and encourages further secretion, thereby causing a rise in glycoside excretion. Through the interruption of the enterohepatic circulation of the cardiac glycosides in yellow oleander, multiple doses of activated charcoal improves outcome in yellow oleander poisoning [9].

Antidote

Anti-digoxin Fab fragments are a safe and effective treatment for serious cardiac arrhythmias induced by yellow oleander.[10] The investigators used 1200mg of antidigoxin Fab fragment in a randomized controlled trial involving 66 patients. Flanagan RJ and Jones AL recommends that the approximate dose of Fab fragments (mg) is 80 times the digoxin body burden (mg). They recommend a dose of 380mg of anti-digoxin Fab fragment in an adult if neither the dose ingested nor the plasma digoxin / digitoxin concentration is known. The dose for elderly patients or those with renal impairment should be similar to that for those with normal renal function. The antibody fragments are given intravenously over 15-30 minutes after dilution to at least 250ml with 0.9% (w/v) sodium chloride. Fab fragments are generally well tolerated. Adverse effects include hypokalemia and exacerbation of congestive cardiac failure; renal function could be impaired in some patients.[25] Indications of use include hyperkalemia (>5.0meq/l), life-threatening supraventricular and ventricular dysrhythmias and hemodynamically significant bradycardia unresponsive to atropine.[18]

Treatment of arrhythmias

Since onset of action of Fab fragments may take 30-60min, intervening treatment of significant complications should be done.

Bradydysrhythmias

Atropine and cardiac pacing can be tried. Patients requiring transcutaneous cardiac pacing should receive Fab fragments prior to it. Transvenous pacing and use of isoproterenol can result in degeneration of cardiac rhythm and should be avoided. Overdrive pacing should not be used for the control of ventricular dysrhythmias.[18]

Tachydysrhythmias

Phenytoin and lidocaine are agents of choice. Magnesium has been reported to reverse digoxin induced dysrhythmias and may be useful as long as anuric renal failure is not present. Quinidine and procainamide may enhance cardiac glycoside toxicity by slowing conduction across AV node; both should be avoided.[18]

Cardioversion is used as a last resort, as it may induce intractable ventricular fibrillation. Fab fragments should be given with cardioversion. If time permits, cardioversion should be attempted after a loading dose of phenytoin and at a significantly reduced initial power setting of 5-10J.[18]

Hyperkalemia

Glucose, insulin, sodium bicarbonate and salbutamol may be used to facilitate redistribution of potassium intracellularly. However, salbutamol may precipitate cardiac dysrhythmias. Life-threatening hyperkalemia should be treated with Fab fragments. Calcium should be avoided in hyperkalemia due

to cardiac glycoside toxicity as already there is excess of calcium intracellularly and results in overloading of myocytes with calcium, increased dysrhythmias, and a higher rate of death.[18]

Cardiac arrest

Give 10-20 vials of Fab and treat with standard advanced cardiac life support (ACLS) principles. Prolonged efforts at resuscitation may be warranted until Fab fragments begin to work.[18]

Elimination

Forced diuresis, hemoperfusion and hemodialysis are ineffective in enhancing the elimination of cardiac glycosides due to their large volume of distribution. Hemodialysis will efficiently remove potassium from extracellular fluid.[18]

Analysis of published Indian reports

Analysis of 300 patients of yellow oleander poisoning studied in BS Medical College, Bankura from 1986 to 1990 showed the following.

- Majority i.e., 246 (82%) were females. 226 (75.33%) young in the age group (11-20 years). Delay in taking treatment was between 6 to 8 hrs. Number of seeds ingested varied from ½ to fifteen. 97.33% ingested seeds in the crushed form. 52% were asymptomatic, 30.66% had vomiting and 12% had palpitation. 138 (46%) revealed various

arrhythmias. Sinus bradycardia in 68 cases and ST-T changes present in 39.33%. Number of seeds ingested did not bear any relationship with ECG changes.

- Analysis of clinical profile of 32 cases of yellow oleander poisoning at VSS Medical College, Burla. Majority were females in the age group 16-20 yrs. Symptoms were vomiting in 46.9% of cases, numbness sensation in 43.8%, dryness of mouth in 25%, diarrhea in 18.8% of cases. Routine blood and urine examination were within normal limits. There was no biochemical abnormalities detected. The ECG change noted were sinus bradycardia in 17 (53%), 1° AV block in 5 (15.6%), III° AV block in 1 (3.1%), ST elevation in 2 (6.2%), ST depression in 4 (12.5%) and T wave changes in 6 (18.8% of cases).

AIMS AND OBJECTIVES

1. To find out the incidence of yellow oleander poisoning.
2. To analyse the socio-clinical aspects.
3. To correlate clinical and biochemical data with electrocardiographic changes.
4. To identify the possible risk factors for cardiotoxicity and outcome.

MATERIALS AND METHODS

Setting

Department of Medicine, Government Rajaji Hospital and Madurai Medical College, Madurai. There was no other collaborating department.

Design of study

Prospective study

Period of study

August 2005 to January 2006.

Sample size

Hundred and eleven cases of yellow oleander poisoning that satisfied the inclusion and exclusion criteria.

Selection of study subjects

Yellow oleander poisoning cases who fulfilled the inclusion and exclusion criteria.

Inclusion criteria

1. Those admitted in general medicine wards with history of yellow oleander ingestion during the period of August 2005 to January 2006.

Exclusion criteria

1. Pediatric cases were excluded (<13 yrs of age).
2. Those with underlying severe cardiac, renal or hepatic disease were excluded.
3. Patients who were taking the following drugs –digoxin, diuretics, verapamil, diltiazem, β blockers, ACE inhibitors, amiodarone, calcium and potassium supplements were excluded.

Definitions

The definitions adopted during the study period with reference to selected entities are furnished below.

1. **Cardiotoxicity**

   Yellow oleander poisoning cases were divided into no carditoxicity, some carditoxicity and severe cardiotoxicity groups based on electrocardiographic changes.

   a. **No cardiotoxicity**

      This group included patients whose electrocardiogram showed sinus rhythm or sinus tachycardia only.

   b. **Some cardiotoxicity**

      This group included patients whose electrocardiogram showed any one of the following changes.

      1. Sinus bradycardia.

2. First-degree atrioventricular (AV) block.
3. Mobitz Type–I second-degree atrioventricular (AV) block.
4. Atrial ectopics.
5. ST segment and T wave changes that are characteristic of digitalis effect / toxicity.

c. Severe cardiotoxicity

This group included patients whose electrocardiogram showed any one of the following changes:

1. Sino-atrial (SA) block.
2. Junctional rhythm.
3. Mobitz Type–II second-degree atrioventricular (AV) block.
4. Third-degree atrioventricular (AV) block.
5. Atrioventricular (AV) dissociation.

2. Consumption in empty stomach

This included patients who had not consumed anything for at least 8 hrs before consuming the poison.

3. **First aid at home**

   This refers to method adopted by local people to bring out the poison. The method mostly used was to induce vomiting using salt water, tamarind water, soap water etc.

4. **Serum potassium level**

   Hypokalemia - Defined as serum K^+ less than 3.5meq/l.

   Hyperkalemia - Defined as serum K^+ greater than 5.0meq/l.

Methods

Selected sociodemographic, clinical, biochemical, electrocardiographic and treatment details were collected from the patients and recorded in a proforma.

Sociodemographic data consisted of

- Age
- Sex
- Locality
- Occupation
- Income

Data regarding poisoning comprised of part ingested, quantity of poison, method of ingestion, whether consumption in empty stomach or after food, the intention behind poisoning, time of ingestion, first aid at home, consumption

to admission interval, treatment given, duration of hospital stay and the type of outcome.

Clinical date comprised of

Symptom analysis, pulse rate, rhythm, blood pressure and systemic examination.

Laboratory data included

- Blood sugar
- Blood Urea
- Serum Creatinine
- Serum Na^+, K^+, Cl^-, HCO^-_3 values
- Electrocardiogram (ECG)

Blood urea, sugar, serum creatinine and serum Na^+, K^+, Cl^- and HCO^-_3 values were estimated using ERBA XL300 automated analyzer. The blood urea, sugar, creatinine and serum Na^+, K^+, Cl^-, HCO^-_3 were measured at the time of admission before instituting treatment. 12 lead ECG, including rhythm strip in leads II and V_1 was taken in all patients. 12 lead ECG including rhythm strip was taken at admission before instituting treatment and repeated depending on the clinical status.

Ethical committee approval

The present project was approved by the ethical committee.

Consent

An informed consent was obtained from all patients who were included in the study.

Limitations

1. Continuous ECG monitoring and serial levels of electrolytes especially serum potassium could not be done due to technical constraints.
2. Estimation of cardiac glycoside level was not done due to nonavailability and financial constraints.
3. Activated charcoal, anti-digoxin Fab fragments were not administered and temporary pacemaker not used due to financial and technical constraints.
4. Arterial blood gas analysis was not done due to nonavailability at the time of the study.

Conflicts of interest

There was no conflict of interest.

Financial support

Nil

Statistical analysis

Data were entered in Microsoft Excel spreadsheet and analysed utilizing the software-Epidemiological Information Package 2002 (Epi Info 2002) – developed by the Centre for Disease Control and Prevention, Atlanta

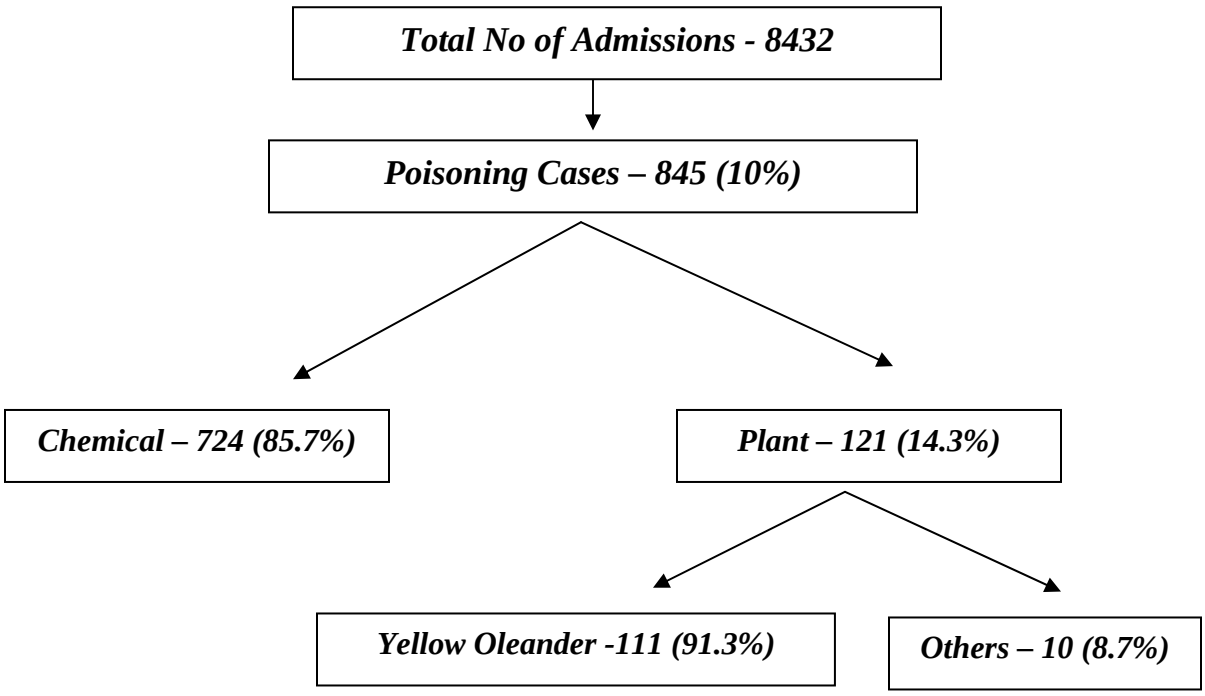
for World Health Organisation. Frequencies, percentages, range, mean, standard deviation and ‘p’ values were calculated using this package.

Chi Square test was done to find out the significance of relationship between the groups. Since the variances were not homogenous, KRUSKULWALLY (X^2 test) was used to find out the significance of difference. The difference was considered to be significant if the ‘p’ value was less than 0.05.

RESULTS

Incidence of Yellow Oleander Poisoning

The incidence of yellow oleander poisoning among total number of admissions in general medicine wards of Government Rajaji Hospital, Madurai during the study period was 13.2 per 1000 admissions. It accounted for 91.7% of the cases of plant poisoning. In general, 10% of the cases among the total number of admission in general medicine wards were poisoning cases. Among the poisoning cases, 85.7% were chemical poisoning and 14.3% plant poisoning. Among the total number of poisoning cases, yellow oleander accounted for 13.1% of the cases. This is explained using a flow chart.



Distribution of cases in relation to age

The maximum number of cases occurred in the age group 20-29 (50.5%) followed by age group 13-19 (21.6%) and 30-39 (16.2%) respectively. The age of the patients ranged from 13-62 years. The mean age and standard deviation was 27.05±9.76. The mean age of poisoning among males was 27.96±9.6 and that of females 26.31±9.91. The difference in the mean age of males and females was not statistically significant (p=0.2458). The graph gives the distribution of cases according to age group.

Distribution of cases in relation to gender

Among the total of 111 cases, 50 (45.05%) were males and 61 (54.95%) were females. The ratio of females : males was 1.22:1, but the difference was not statistically significant (p=0.56).

Distribution of cases in relation to income

72.5% of the patients who were earning had income below Rupees two thousand per month. The mean income was Rupees 2105.31±3623.13, range being Rs. 200 – 30,000. The details are given in the table below.

Table No. 1 Distribution of cases in relation to income

Monthly Income In Rs.	No	%
<1000	28	25.2
1000 – 1999	30	27
2000-2999	11	9.9
3000-3999	4	3.6
4000 and above	7	6.3
Not earning	31	27.9

Intention behind poisoning

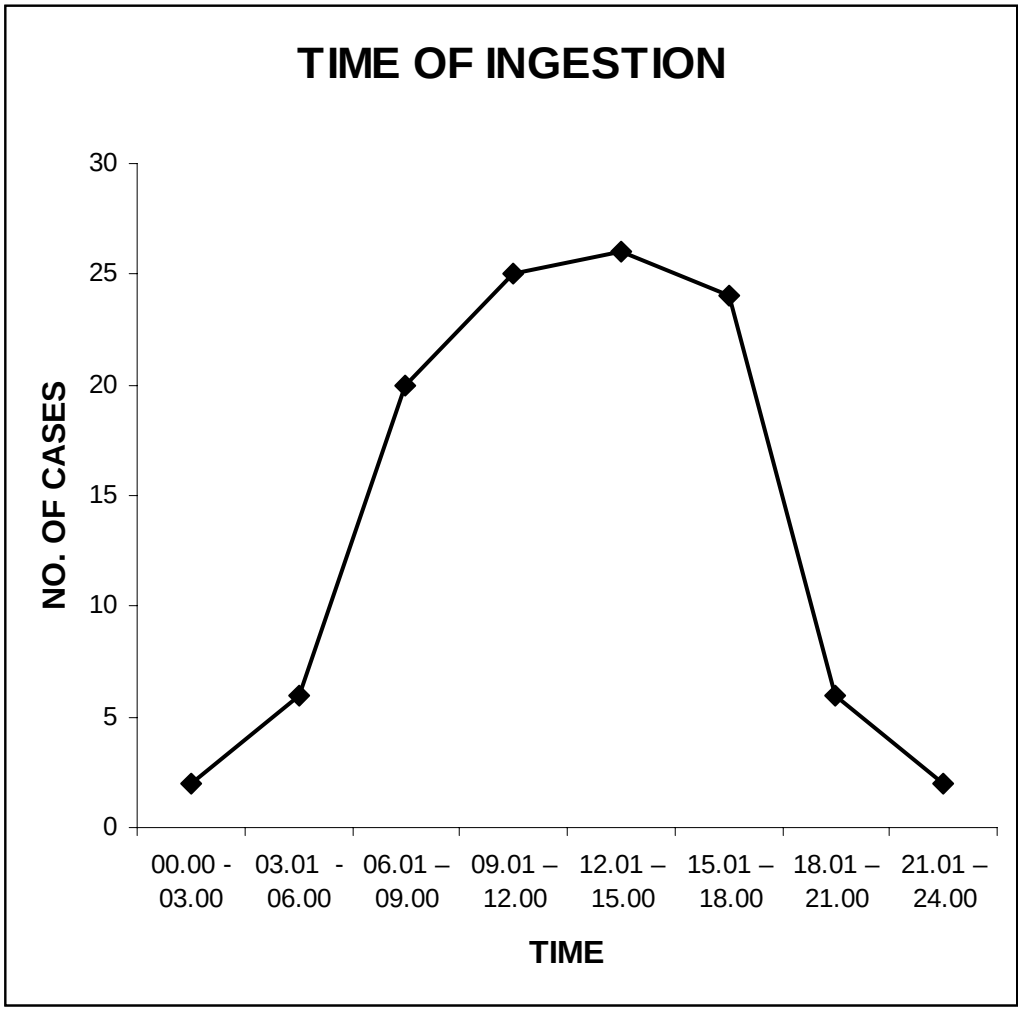
The intention behind poisoning was suicidal in majority of cases (82.9%) and accidental in 1.8%. In 15.3% of cases, the poisoning attempt was done just to frighten others for some personal gain or to resolve conflict. There were no cases of homicidal poisoning.

Table No. 2 Intention behind poisoning

Intention behind poisoning	No. of cases (%)
Suicidal	90 (82.9%)
Accidental	2 (1.8%)
Homicidal	-
Others	19 (15.3%)
Total	111 (100%)

Time of ingestion

As you can see in the graph, in majority of cases (85.5%) the poisoning between 6am – 6pm.



Electrocardiographic manifestations of yellow oleander poisoning

The most common abnormal findings were sinus bradycardia (33.6%) and ST-T changes (41.8%) (which were similar to that described for digoxin effect / toxicity). Sino-atrial block, third-degree AV block and first-degree AV

block were noted in 7 cases each. Mobitz type –II second-degree AV block which is not described in digitalis toxicity occurred in two cases. Depending on the ECG changes all cases of yellow oleander poisoning were divided into no, some and severe cardiotoxicity groups (Refer definitions in materials and methods). In majority of the cases (61.8%) some form of cardiotoxicity was present. Severe cardiotoxicity was present in about $1/5^{th}$ of the cases. The details are depicted below in the table and the pie diagram.

Table No. 3 ECG changes in yellow oleander poisoning

Cardiotoxicity	ECG changes	Cases	
		No.	%
No	Sinus rhythm	36	32.7
	Sinus tachycardia	6	5.5
Some	Sinus bradycardia	37	33.6
	Atrial ectopics	1	0.9
	ST-T changes (digoxin effect/toxicity)	46	41.8
	First-degree AV block	7	6.4
	Mobitz type I second-degree AV block	2	1.8
Severe	Sino-atrial (SA) block	7	6.4
	Junctional rhythm	3	2.7
	Mobitz Type II second-degree AV block	2	1.8
	Third-degree AV block	7	6.4
	AV dissociation	2	1.8

Relationship between part ingested and cardiotoxicity

Majority of the patients had taken either the fruit or seed, 52.8% and 44.6% respectively. 3 of the patients had taken the outer fleshy covering of the nut alone and these patients had no cardiotoxicity. There was no statistically significant difference in the cardiotoxicity caused by fruit and seed (p=0.9582). The details are given in the table given below.

Table No. 4 Part ingested and Cardiotoxicity

Part ingested	Cardiotoxicity					
	No cardiotoxicity		Some cardiotoxicity		Severe cardiotoxicity	
	No.	%	No.	%	No.	%
Fruit	20	48.8	27	57.4	10	50
Seed	18	43.9	20	42.6	10	50
Flower	-	-	-	-	-	-
Leaves	-	-	-	-	-	-
Root	-	-	-	-	-	-
Other parts	3	7.3	-	-	-	-

Relationship between quantity of poison ingested and cardiotoxicity

The mean number of seeds / fruits ingested in no cardiotoxicity group was 2.33 and that in severe cardiotoxicity group was 3.85. The difference was statistically significant (p=0.0001). The range, mean and standard deviation of quantity of poison in each of the groups is depicted in the table and the graph.

Table No. 5 Quantity of poison ingested and cardiotoxicity

Cardiotoxicity	Range	Mean	Standard Deviation
No cardiotoxicity	1-5	2.33	1.65
Some cardiotoxicity	1-10	3.47	1.54
Severe cardiotoxicity	1-18	3.85	1.93
Total	1-18	3.26	2.27

Relationship between method of ingestion of poison and cardiotoxicity

The method of ingestion of poison was crushed in 50.5% of the cases, chewed in 40.5% and swallowed in 9%. 76.8% of those who had taken the poison in the crushed form had some form of cardiotoxicity compared to 50% in those who had taken the poison chewed. The difference between the groups was statistically significant (p=0.0001). The details are shown in the table below.

Table No. 6 Method of ingestion and cardiotoxicity

Method of ingestion	Cardiotoxicity							
	No cardiotoxicity		Some cardiotoxicity		Severe cardiotoxicity		Total	
	No	%	No	%	No	%	No	%
Crushed	13	23.2	32	57.1	11	19.7	56	100
Chewed	22	50	14	31.8	8	18.2	44	100
Swallowed	7	70	2	20	1	10	10	100

Relationship between manner of consumption and cardiotoxicity

60.4% of the patients had consumed the poison in empty stomach and the rest after food. 70.2% of the patients who had taken the poison in empty stomach had some form of cardiotoxicity compared to 48.8% in patients who took the poison after food. The difference between the groups was statistically significant (p=0.041). The details are shown in the graph and the table given below.

Table No. 7 Manner of consumption and cardiotoxicity

Manner of consumption	Cardiotoxicity							
	No cardiotoxicity		Some cardiotoxicity		Severe cardiotoxicity		Total	
	No	%	No	%	No	%	No	%
In empty stomach	20	29.8	35	52.5	12	18.0	67	100
After food	22	51.2	13	30.2	8	18.6	43	100

Relationship between first aid and cardiotoxicity

Majority were not given first aid (57.7% of cases). 59.6% of patients who were given first aid developed some form of cardiotoxicity compared to 63.5% in patients who were not given first aid (Refer definitions in materials and methods). The difference between the groups was not statistically significant (p=0.8529). The details are given in the table below.

Table No. 8 First aid and cardiotoxicity

First aid	Cardiotoxicity							
	No cardiotoxicity		Some cardiotoxicity		Severe cardiotoxicity		Total	
	No	%	No	%	No	%	No	%
Given	19	40.4	20	42.5	8	17.1	47	100
Not given	23	36.5	28	44.4	12	19.1	63	100

Relationship between time of first aid and cardiotoxicity

In patients who were given first aid 2 hrs after consumption of poison, all of them developed cardiotoxicity compared to 48.4% in patients who were given first aid within one hour. The mean time of first aid in no, some and severe cardiotoxicity groups were 34.4 min, 112.9 min and 132.5 min respectively. The difference between the groups was statistically significant (p=0.0038). The details are given in the table below and explained using a graph.

Table No.9 Time of first aid and cardiotoxicity

Time of first aid	Cardiotoxicity							
	No cardiotoxicity		Some cardiotoxicity		Severe cardiotoxicity		Total	
	No	%	No	%	No	%	No	%
1-60 minutes	16	51.6	11	35.5	4	12.9	31	100
61-120 minutes	3	37.5	4	50.0	1	12.5	8	100
>120 minutes	-	-	5	62.5	3	37.5	8	100
Range	10-120 min.		5-390 min		30-420 min.			
Mean	34.4 min		112.9 min		132.5 min			
S.D	32.5		126.7		126.1			

Relationship between consumption to admission interval and cardiotoxicity

The mean delay in getting admitted to Government Rajaji Hospital (GRH), Madurai after consumption of poison was 12.72±4.6 hrs, the range being 1-62 hrs. The mean delay in no, some and severe cardiotoxicity group was 13.32, 12.25, and 12.36 hrs respectively. The difference between the groups was not statistically significant (p=0.6012). The details are given in the table below.

Table No. 10 Consumption to admission interval and cardiotoxicity

Time interval between consumption to admission (in hrs)	Cardiotoxicity			Total
	No cardiotoxicity	Some cardiotoxicity	Severe cardiotoxicity	
Range	1-62	1-61.5	1.25-20.25	1-62
Mean	13.32	12.25	12.36	12.72
S.D.	4.38	4.73	4.92	4.6

Relationship between symptoms and cardiotoxicity

The most common symptoms of yellow oleander poisoning were vomiting (73%), numbness of tongue and lips (57.7%), giddiness (56.8%) and diarrhea (27.9%). The relationship between three symptoms, i.e., vomiting, diarrhea, altered mental status with cardiotoxicity was analysed. In those patients who did not have any one of the above three symptoms, only 27.3% had features of cardiotoxicity. In those patients who had at least one of the three symptoms, 66.7% had features of cardiotoxicity. Approximately 75% of the patients who had at least two symptoms or all the three symptoms had features of cardiotoxicity. The difference between the groups was statistically significant (p=0.0005). The details are shown in the tables given below.

Table No. 11 Symptoms of yellow oleander poisoning

Symptoms	No	%
Vomiting	81	73
Abdominal pain	19	17.1
Diarrhea	31	27.9
Giddiness	63	56.8
Numbness of tongue & lips	64	57.7
Altered mental status	19	17.1
Blurred vision	21	18.9
Palpitation	23	20.7
Shortness of sheath	8	7.2

Table No.12 Symptoms and cardiotoxicity

Presence of symptoms	Cardiotoxicity							
	No cardiotoxicity		Some cardiotoxicity		Severe cardiotoxicity		Total	
	No	%	No	%	No	%	No	%
Vomiting (80)	24	30	39	48.75	17	21.25	80	100
Diarrhoea (31)	7	22.58	15	48.38	9	30.03	31	100
Altered (18) mental status	5	27.78	9	50	4	22.22	18	100
None of the above three symptoms	16	72.7	4	18.2	2	9.1	22	100
Atleast one symptom	17	33.3	26	51.0	8	15.7	51	100
Atleast two symptoms	8	24.25	17	51.5	8	24.25	33	100
All the three symptoms	1	25	1	25	2	50	4	100

Vital signs and biochemical parameters

The range, mean and standard deviation values of pulse rate, blood pressure and biochemical parameters are given in the table below. The mean values of all these parameters were within normal limits. Pulse rate was irregular at admission in 16.2% of the cases, in the rest the pulse rate was regular. Hypotension was present in two cases at admission.

Table No.13 Vital signs and biochemical parameters

Parameter	Range	Mean	S.D
Pulse rate at admission	36-140	80.07	20.9
Systolic blood pressure (mmHg)	70-150	111.8	18.63
Diastolic blood pressure (mmHg)	40-100	73.75	10.57
Blood urea (mg/dl)	15-72	27.19	10.33
Blood sugar (mg/dl)	56-235	91.54	31.77
Serum Creatinine (mg/dl)	0.6-1.8	0.9	0.32
Na^+ (meq/l)	122-160	138.44	5.23
Cl^- (meq/l)	90-106	97.69	2.83
HCO_3^- (meq/l)	15-24	19.33	1.84

Relationship between serum potassium values and cardiotoxicity

Serum potassium levels was measured at time of admission in 97 out of 111 cases. Out of these only two cases had hyperkalemia, 7 cases had hypokalemia and in the majority (90.7%) serum potassium values were within normal limits. The mean serum potassium value in no, some and severe cardiotoxicity groups were 3.85, 4.09 and 4.16 meq/l respectively. The difference between the groups was statistically significant (p=0.0201). The details are given in the two tables shown below and explained using a graph.

Table No. 14 Serum potassium levels and cardiotoxicity

Cardiotoxicity	**Serum potassium values**		
	Range (meq/l)	**Mean (meq/l)**	**Standard Deviation (S.D.)**
No cardiotoxicity	3-4.6	3.85	0.38
Some cardiotoxicity	3.4-5.6	4.09	0.43
Severe cardiotoxicity	3.5-4.9	4.16	0.40
Total	3-5.6	4.01	0.42

Table No.15 Serum K^+ levels in yellow oleander poisoning

Serum K^+ (meq/l)	No. of cases	%
<3.5	7	7.2
3.5-5	88	90.7
>5	2	2.1

Relationship between gastric lavage and cardiotoxicity

Gastric lavage was given in 90.9% of the cases. In those who were given gastric lavage, 39.0% did not develop any cardiotoxicity compared to 33.3% in those who were not given gastric lavage. The difference between the groups was statistically insignificant (p=0.5675). The table below shows the details.

Table No.16 Gastric lavage and cardiotoxicity

Gastric lavage	Cardiotoxicity							
	No cardiotoxicity		Some cardiotoxicity		Severe cardiotoxicity		Total	
	No	%	No	%	No	%	No	%
Given	39	39.0	43	43.0	18	18.0	100	100
Not given	3	33.3	4	44.5	2	22.2	9	100

Treatment given in yellow oleander poisoning

Most of the patients were given supportive treatment in the form of gastric lavage, injection atropine and tablet orciprenaline. Steroids were used in 46.8% of cases. Some patients were given tablet salbutamol and tablet deriphylline. Few patients received injection sodium bicarbonate. The details are given in the table given below.

Table No. 17 Treatment given in yellow oleander poisoning

Treatment	No. of cases	
	No	%
Gastric lavage	100	90.9
Injection atropine	78	71.6
Tablet orciprenaline	97	88.2
Steroids	52	46.8

Relationship between cardiotoxicity and duration of hospital stay

The mean duration of hospital stay was 4.55 days, range being 1-9 days. The mean duration in no, some and severe cardiotoxicity groups was 3.64, 4.96 and 5.65 days respectively. The difference between the groups was statistically significant (p=0.0001). The details are given in the table below and explained using a graph.

Table No. 18 Duration of hospital stay and cardiotoxicity

Duration of hospital stay	**No cardiotoxicity**	**Some cardiotoxicity**	**Severe cardiotoxicity**	**Total**
Mean	3.64	4.96	5.65	4.55
S.D.	1.62	1.03	1.35	1.57
p	0.0001			
Range	1-9			

Outcome

Out of 111 cases, 86.4% of the cases were discharged well. Death occurred in two cases (1.9%, one male and female patient) and 11.7% of the patients absconded from the wards. There was no statistically significant difference in outcome among males and females (p=0.7002).

Table No. 19 Outcome

Outcome	Cases					
	Male		Female		Total	
	No.	%	No.	%	No.	%
Discharged well	41	82	55	90.2	96	86.4
Expired	1	2	1	1.6	2	1.9
Absconded	8	16	5	8.2	13	11.7
Total	50	100	61	100	111	100

Relationship between cardiotoxicity and outcome

Out of 111 cases, only two deaths occurred. The deaths occurred in patients who had severe cardiotoxicity. But there was no statistically difference in outcome among no, some and severe cardiotoxicity groups (p=0.6182).

Table No. 20 Cardiotoxicity and outcome

Outcome	Cardiotoxicity					
	No cardiotoxicity		Some cardiotoxicity		Severe cardiotoxicity	
	No.	%	No.	%	No.	%
Discharged well	31	73.8	46	95.8	19	90.5
Expired	-	-	-	-	2	9.5
Absconded	11	26.2	2	4.2	-	-

DISCUSSION

Yellow oleander poisoning is a common method of deliberate self-harm among young adults in Srilanka and southern India. This study was done to find out the burden of this poisoning among admissions in general medicine wards of Government Rajaji Hospital, Madurai, to analyse the socio-clinical aspects, to correlate clinical and biochemical parameters with cardiotoxicity and to identify the possible risk factors for cardiotoxicity and outcome.

The incidence of yellow oleander poisoning among total number of admissions in general medicine wards of our hospital during the study period was 13.2 per 1000 admissions. Though it has been mentioned in previous studies that thousands of cases occur in Srilanka every year[4], the exact incidence in a particular population has not been previously reported.

Among the 111 cases studied, the mean age of patients was 27.05±9.76 years, range being 13-62 years (pediatric cases not included). 71.7% of the cases occurred in the age group between 13-29 years. This observation confirms the observation of previous Indian and Srilankan studies that yellow oleander poisoning was found commonly among adolescents and young adults[4,7]. Eddleston M et al, in a study of 415 cases in Srilanka observed that

the patients were young (mean age 25.8 years, range 11-71). In that study more than 50% of women and 35% of men were under 21 years[4].

Regarding the sex distribution 54.95% of the cases were females and 45.05% cases were males, the ratio being 1.22:1. In the present study there was only a slight female preponderance when compared to findings of previous Indian and Srilankan studies. Eddleston M et al, observed a female : male ratio of 1.6:1 in his study involving 415 patients in Srilanka[4]. Generally this poisoning was found to be more common among females when compared to males [4,7,25].

Majority of the patients belonged to the upper lower and lower socioeconomic class [Kuppuswami, 1962 (modified)]. 72.5% of the patients who were earning had income below Rupees two thousand per mth. 70% of the patients were daily wage labourers.

70% of the patients were from the rural areas probably due to the fact that the plant was easily available and widely grown in rural areas. There was no expenditure of money in consuming the poison and for many patients this was only poison known to them.

Most of the cases occurred during the working hours 6am – 6pm (85.5%) when the relatives were away for work or the victims have consumed the poison near their workplace.

The intention behind the poisoning was suicidal in 82.9% of the cases. The reasons included interpersonal conflict, unemployment, failure to achieve goal, situational reaction, grief reaction, physical illness etc. One patient had underlying psychiatric illness, schizophrenia. In 15.3% of the patients, poisoning attempt was done just to frighten others for some personal gain or to resolve conflicts. There were two cases of accidental poisoning among adolescents. There were no cases of homicidal poisoning probably due to the bitter taste of the poison. The observations regarding the intention behind poisoning were similar to that observed by Eddleston M et al [4].

Regarding underlying illness, except for three patients, one case of schizophrenia, one case of old anteroseptal myocardial infarction, one case of hypertension, none had any previous illness. All the three patients were on irregular treatment. Four of the female patients were pregnant while consuming the poison and all of them recovered. This was similar to the findings observed by Eddleston M et al, who noted that only one patient had underlying illness (rheumatic heart disease)[8]. This observation differed markedly from patients with digoxin poisoning. Many of the patients with

digoxin poisoning had underlying heart disease and were on multiple drugs [27]. This observation is important because as a result of young age and previously healthy state, the cardiac arrhythmias induced by yellow oleander poisoning are unlikely to result from pre-existing conditions.

The electrocardiographic changes that were noted in this study was mainly due to depressed conduction. Most common abnormalities were sinus bradycardia, ST-T changes suggestive of digoxin effect / toxicity, first-degree AV block, third-degree AV block and sino-atrial block. Others included second-degree AV block, junctional rhythm, AV dissociation and atrial ectopics. The observations were similar to that of Eddleston M et al except that tachyarrhythmias (0.5-1%) like atrial flutter, atrial fibrillation, ventricular tachycardia and ventricular fibrillation observed by Eddleston M et al were not observed in the present study. In the same study 3-6% had supraventricular tachycardia and 2% had ventricular ectopics which was not observed in the present study[8]. Mobitz type – II second-degree AV block which is not described in digoxin toxicity occurred in two cases[28]. In yellow oleander poisoning arrhythmias due to depressed conduction were more common than tachyarrhythmias and thus differs from digoxin poisoning in which tachyarrhythmias were found to be more common [27].

Depending on the ECG changes patients were divided into no, some and severe cardiotoxicity groups and the relationship between various factors and cardiotoxicity was studied (Refer definitions in materials and methods). Majority (61.8%) of cases showed some form of cardiotoxicity. Severe cardiotoxicity was present in approximately 20% of the cases.

The common method of poisoning in the present study was ingestion of fruits or seeds in the crushed or chewed form. Three patients had taken the outer fleshy covering of the nut and these patients had no cardiotoxicity. Toxicological studies in albino rats have shown that all parts of the plant were poisonous especially the seeds / kernels of fruit[16]. Other parts like roots, leaves or flowers were not taken. The mean number of seeds / fruits ingested in severe (3.85) and some cardiotoxicity groups were (3.47) higher than that in no cardiotoxicity group (2.33). The range in no, some and severe cardiotoxicity groups were 1-5, 1-10, and 1-18 (seeds/fruits) respectively. Although there was a positive correlation between quantity of poison and cardiotoxicity in the present study it should be noted that even one seed / fruit was found to cause some or severe cardiotoxicity. Relationship between quantity of poison and outcome was not present as only two deaths had occurred and patients who had taken six and ten seeds had all survived. Two patients who died had consumed 5 and 18 seeds respectively. Eddleston M et

al (1999) also observed no relationship with seeds ingested and outcome. In that study six patients who had died had consumed 10,5,8,1,5 and 2 seeds[4]. So the quantity of poison alone cannot determine outcome, it may be influenced by other factors like method of ingestion, consumption in empty stomach or not, delay in gastric lavage, treatment given etc.

Majority had taken the seeds / fruits in the crushed form. There was a higher incidence of cardiotoxicity in those who had taken the seeds / fruits crushed compared to those who had chewed or swallowed the poison. This is probably due to the fact that more amount of cardiac glycoside is available to be absorbed once the seeds/fruits are crushed. In seven patients who had swallowed the seeds, two patients developed some cardiotoxicity and one patient developed severe cardiotoxicity. This finding is supported by the fact that in Srilanka people usually eat the seeds whole and they develop cardiotoxicity. So even the seeds taken as a whole can cause cardiotoxicity but to a lesser extent when compared to crushed or chewed form. The method of ingestion observed in the present study was similar to that reported in a study from Eastern India in which majority (97.33%) of the patients had ingested the poison in the crushed form[7].

Most of the patients (60.4%) had consumed the poison in empty stomach. There was a higher incidence of cardiotoxicity in patients who had

consumed the poison in empty stomach than after food. This is probably due to the fact that absorption of cardiacglycoside is better in empty stomach. In previous studies this relationship was not assessed.

In 42.3% of cases first aid was given at home after the ingestion of poison. The commonly used method was to induce vomiting using soap water, tamarind water, salt water etc. There was no statistically significant difference in cardiotoxicity between patients who were given first aid and those who were not given first aid. This is because of the fact that in many patients there was a delay in giving first aid. But in patients who were given first aid, delay in giving first aid was associated with increased incidence of cardiotoxicity. So bringing out the poison early before the poison has passed into intestine reduces the incidence of cardiotoxicity in yellow oleander poisoning. The relationship between time of first aid and cardiotoxicity was not studied in previous reports.

The mean delay in getting admitted to Government Rajaji Hospital, Madurai after consumption of poison was 12.72 ±4.6 hrs, the range being 1-62 hrs. A correlation between delay in getting admitted to our hospital and cardiotoxicity could not be obtained probably due to the fact that many patients were given first aid and treated outside in other hospitals/institutions before being referred to our hospital. Bose TK et al (1999) observed a delay of

6-8 hrs[7]. The reasons for the delay in getting admitted to our hospital in the present study would be treatment of patients outside by others doctors and lack of adequate transportation in interior rural areas. In patients with high suicidal intent the relatives come to know of the poisoning only after several hours and this might have contributed to the delay.

The most common symptoms of yellow oleander poisoning in the present study were vomiting (73%), numbness of tongue and lips (57.7%), giddiness (56.8%) and diarrhea (27.9%). This was similar to findings noted by Saravanapavananthan N and Ganeshmoorthy J (1986) who observed vomiting, giddiness and diarrhea as the most common symptoms in their study of 170 cases in Srilanka[2]. Patients who had either vomiting, diarrhea or altered mental status had higher incidence of cardiotoxicity compared to those who did not have any one of the above symptoms. Among patients who had at least two or all the three of above symptoms 75% developed cardiotoxicity. Thus patients with either vomiting, diarrhea or altered mental status should be closely monitored for cardiotoxicity. Ellenhorn and Barceloux (1988) have also noted that in severe poisoning diarrhea and vomiting are early features[20].

The average pulse rate at admission was 80.07±20.9 per minute, range being 36-140 per minute. Many patients had a normal pulse rate and rhythm at admission only to develop features of cardiotoxicity later usually within a day.

Eddleston M et al (1999) has described a patient who remained in sinus rhythm for three days before developing second degree AV block[4]. So patients may have to be observed for 3-4 days after ingestion of poison before being discharged home.

Hyperkalemia occurs in severe yellow oleander poisoning[8]. Severe hyperkalemia can contribute to atrioventricular (AV) block and depressed myocardial excitability[19]. In the present study hyperkalemia was noted in only two out of 97 cases (2.1%) in whom the serum potassium levels were measured. Both of these patients had some cardiotoxicity. But there was a correlation between serum potassium levels and cardiotoxicity in the present study. The mean serum potassium values were higher in some (4.09meq/l) and severe cardiotoxicity groups (4.16meq/l) compared to patients with no cardiotoxicity (3.85meq/l). Eddleston M et al (2000) noted hyperkalemia in 38 patients out of 118 cases (32.2%). Very high values of potassium like 7.2meq/l, 8.4meq/l and 10.8meq/l were observed in that study[8]. In the present study the two patients who had hyperkalemia had values of 5.6 and 5.1meq/l. The reason why hyperkalemia was not as common when compared to Srilankan study would be that poisoning might have been less severe or due to the persistent vomiting due to poisoning per se or due to induced emesis. Another reason would be that serial serum potassium measurements were not

obtained due to technical constraints and hyperkalemia developing during the course of poisoning was missed (serum potassium levels were measured only at admission). Moreover the baseline potassium level in the population also was not known. Hypokalemia was noted in 7 of our cases. Eddleston M et al, (2000) noted hypokalemia in 9 out of 118 cases[8]. Hypokalemia may be probably due to persistent vomiting due to poisoning per se or due to induced emesis. Hypokalemia can exacerbate cardiac glycoside toxicity as if facilitates enhanced binding of cardiac glycosides to Na^+ -K^+ ATPase pump[22]. Both hyperkalemia and hypokalemia are dangerous in yellow oleander poisoning and serial monitoring of potassium levels and adequate treatment is necessary. Severe hyperkalemia may require treatment with antidigoxin Fab fragments[18].

There was no statistically significant difference in cardiotoxicity between patients who were given gastric lavage and those who were not given gastric lavage. Gastric lavage is most useful when started within 60 minutes after ingestion[24]. Early gastric lavage is more important than whether gastric lavage is given or not in reducing the incidence of cardiotoxicity. This relationship was not assessed in previous published reports.

Most of the patients were treated with supportive measures like gastric lavage, injection atropine, tablet orciprenaline and in about 50% of the cases steroids were used. There are no scientific studies or trials to support the use

of steroids in yellow oleander poisoning. Activated charcoal, temporary cardiac pacing and antidigoxin Fab fragments were not used due to economical and technical constraints.

The mean duration of hospital stay in the present study was 4.55 days, range being 1-9 days. Those patients with some and severe cardiotoxicity had increased duration of hospital stay when compared to patients with no cardiotoxicity. This was similar to findings observed by Bose TK et al (1999) who observed a median hospital stay of 5 days[7].

Death occurred in two cases (one male and female patient) within one hour after admission. The male patient had atrioventricular dissociation while the female patient died before ECG could be taken. The case fatality rate was 1.9%. Bose TK et al (1999) observed a case fatality rate of 4.6% among 300 patients in eastern India[7]. In Srilankan studies, Eddleston M et al observed a case fatality rate of approximately 10%[4]. The lower case fatality rate in the present study may be due to less severe poisoning in Tamilnadu when compared to that in Srilanka and probably due to lesser number of patients studied. As the deaths were very few, there was no statistically significant difference in outcome among no, some and severe cardiotoxicity groups and also there was no statistically significant difference in outcome among male and female patients.

Areas of further work

1. The efficacy of anti–digoxin Fab fragments in treating serious cardiac arrhythmias induced by yellow oleander has been established by Eddleston M et al (2000) in the only small randomised clinical trial involving 66 patients[10]. Further studies are required to confirm the efficacy of anti-digoxin Fab fragments in treating serious cardiac arrhythmias induced by yellow oleander.
2. Multiple doses of activated charcoal was found to be safe and more effective than single dose activated charcoal in reducing death and life threatening cardiac arrhythmias after yellow oleander poisoning in the only single–blind, randomised, placebo-controlled trial in Srilanka[9]. Further studies are required to confirm the superiority of multiple doses of activated charcoal over single dose activated charcoal in yellow oleander poisoning.
3. Focal myocardial edema has been noted in cases of yellow oleander poisoning[7]. So studies can be taken up to assess whether glucocorticoids have any role in improving outcome in this poisoning.

CONCLUSIONS

1. The incidence of yellow oleander poisoning in general medicine wards of Government Rajaji Hospital, Madurai during the study period was 13.2 per 1000 admissions.

2. Yellow oleander poisoning was most commonly observed among young adults and adolescents.

3. Although there was a slight female preponderance the difference was not statistically significant.

4. Most of the patients were from rural areas belonging to upper lower and lower socio-economic class.

5. Most of the cases occurred during day time (6am – 6pm).

6. In majority of cases, the intention was suicidal secondary to interpersonal conflict, grief reaction, situational reaction, unemployment etc.

7. The most common symptoms of yellow oleander poisoning in the present study were vomiting, numbness of tongue and lips, giddiness and diarrhea.

8. Electrocardiographic changes that were noted were mainly due to depressed conduction. Most common abnormalities were sinus bradycardia, ST-T changes similar to digoxin effect / toxicity, first-degree AV block, third-degree AV block and sino-atrial block.

9. Hyperkalemia as a manifestation of yellow oleander poisoning was uncommon in the present study compared to Srilankan studies.

10. There was a higher incidence of cardiotoxicity as the quantity of poison increased but even ingestion of one seed / fruit was found to cause severe cardiotoxicity.

11. There was a higher incidence of cardiotoxicity in those who had taken the seeds / fruits crushed when compared to those who had chewed or swallowed the poison.

12. Cardiotoxicity was found to be higher in patients who had consumed the poison in empty stomach than after food.

13. Delay in inducing emesis or giving gastric lavage was associated with increased incidence of cardiotoxicity.

14. The occurrence of cardiotoxicity was higher in patients who had vomiting, diarrhea or altered mental status compared to patients who did not have any of these symptoms.

15. The mean serum potassium values at presentation were higher in patients who had cardiotoxicity when compared to patients who had no cardiotoxicity.

16. Case fatality rate was low in the present study when compared to previous Srilankan and Indian studies.

SUMMARY

Yellow oleander poisoning is a common method of suicide in South India and Srilanka with thousands of cases occurring in Srilanka each year at present. This study was undertaken to find out the incidence of yellow oleander poisoning in our hospital, to study the socio-clinical aspects, to find out correlation between clinical and biochemical parameters with electrocardiographic changes and to find out possible risk factors for cardiotoxicity and outcome.

After institutional ethical clearance, with an informed consent and with inclusion and exclusion criteria 111 cases of yellow oleander poisoning were included in the study and were evaluated on social, clinical, biochemical and electrocardiographic aspects. The data were entered in Microsoft Excel spread sheet and analysed statistically.

The incidence of yellow oleander poisoning in general medicine wards of our hospital was 13.2 per 1000 admissions. 54.95% of the cases were females. The mean age of poisoning was 27.05 ± 9.76 years. The intention was suicidal in majority. The most common symptoms were vomiting, numbness of tongue and lips, giddiness and diarrhea. The most common abnormal ECG findings were sinus bradycardia, ST-T changes similar to that

described for digoxin effect/ toxicity, sino-atrial block, first-degree AV block and third-degree AV block. Depending on the ECG changes, patients were decided into no, some and severe cardiotoxicity groups and relationship between various factors and cardiotoxicity analysed. The mean number of seeds / fruits ingested in patients who had cardiotoxicity was higher than in patients who had no cardiotoxicity. Majority had taken the poison crushed and in empty stomach which resulted in greater cardiotoxicity. Delay in inducing emesis or giving gastric lavage was associated with greater cardiotoxicity. The occurrence of cardiotoxicity was higher in patients who had vomiting, diarrhea or altered mental status. The mean serum potassium values at presentation was higher in patients who had cardiotoxicity. Hyperkalemia was noted in only two cases. The mean duration of hospital stay was 4.55 ± 1.57 days and was higher in patients who had cardiotoxicity. The case fatality rate was 1.9%.

Yellow oleander poisoning was found to be a common method of suicide among young adults and adolescents in this part of the country and was slightly more common in females. It accounted for 13.1% of cases among the total number of poisoning cases during the study period. Most of the patients were from rural areas belonging to upper lower and lower socio-economic class. The most common symptoms were vomiting, numbness of

tongue and lips, giddiness and diarrhea. The most common electrocardiographic abnormalities were sinus bradycardia, ST-T changes similar to digoxin effect/toxicity, first-degree AV block, third-degree AV block and sino-atrial block. Hyperkalemia was found to be uncommon when compared to previous Srilankan studies. The occurrence of cardiotoxicity was greater in patients who had taken the poison crushed and in empty stomach, who had taken more quantity of poison, in whom there was a delay in inducing emesis or giving gastric lavage, who had vomiting, diarrhea or altered mental status and who had higher serum potassium levels at admission. The more severe the cardiotoxicity more was the duration of hospital stay. The case fatality rate was low when compared to previous studies.

Although this study could identify the risk factors for cardiotoxicity, the risk factors associated with poor outcome could not be well established as the deaths were very few. Hence further studies are required to identify risk factors associated with poor outcome in this poisoning. Further studies are also required to assess the role of glucocorticoids in improving outcome. The benefit reported with multiple doses of activated charcoal and anti-digoxin Fab fragments also need to be confirmed by further studies.

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APPENDIX II

PROFORMA

SOCIO-CLINICAL, BIOCHEMICAL AND ELECTROCARDIOGRAPHIC ASPECTS OF YELLOW OLEANDER POISONING

Name : Age: Sex: M/F IP No.:

Occupation: Income: Serial No.:

DOA: DOD: Duration of Hospital stay:

Religion: H/M/C/ Others

Marital status: M/UM/ Separated /Divorcee / Widow/ Widower

Address:

Social Profile

Place of Ingestion :

Part ingested : Leaves / Flower / Fruit / Seed /Roots / Others

Quantity of poison :

Method of ingestion : Crushed / Chewed / Swallowed / Others

Mixed with : Water/Oil/Other poison/Alcohol/Food /Others

Consumption in : Empty Stomach / After Food ( )hrs

Intention : Suicidal / Accidental / Homicidal / Others

Reason for ingestion:

Why this poison was preferred over others?

Are there other victims? Yes / no If yes relation to case

Time Profile

Time of ingestion :

Time after which family members / others came to know:

First aid at home : Time :

Treatment by other Doctors: Time :

Time of Admission:

Underlying Psychiatric Disease Yes / No If yes

Other diseases: HIV / Leprosy / Heart disease / PTB / BAsthma / Epilepsy / DM / HT / Jaundice / Others

Women - L.M.P. Pregnant : Yes / No

Clinical profile

GI - Nausea/Vomiting/Abdominal pain/Diarrhea / Anorexia

CNS - Giddiness/Headache/Fatigue/Weakness/Numbness of tongue & lips /Altered mental status / Seizures

Visual - Blurred vision/Scotomas / Flashes of light / Xanthopsia

Cardiac - Palpitations/ Shortness of breath / Chest pain/ Chest discomfort

Physical examination PR Rhythm Volume

BP RR Febrile / Afebrile Dehydration : No / Some / Severe

Pallor / Icterus / Cyanosis / Clubbing / Lymphadenopathy / Pedaledema

CNS: Level of consciousness

Tone Deep Tendon reflexes Plantar

Other systems:

Investigations ECG in all leads with rhythm strip

Date			
Blood urea (mg/dl)			
Sugar (mg/dl)			
Creatinine (mg/dl)			
Na^+ (meq/l)			
K^+ (meq/l)			
Cl^- (meq/l)			
HCO_3^- (meq/l)			

Treatment given

Gastric lavage - Yes / No Psychiatry Opinion

Activated Charcoal - Yes / No

Inj. Atropine - Yes / No

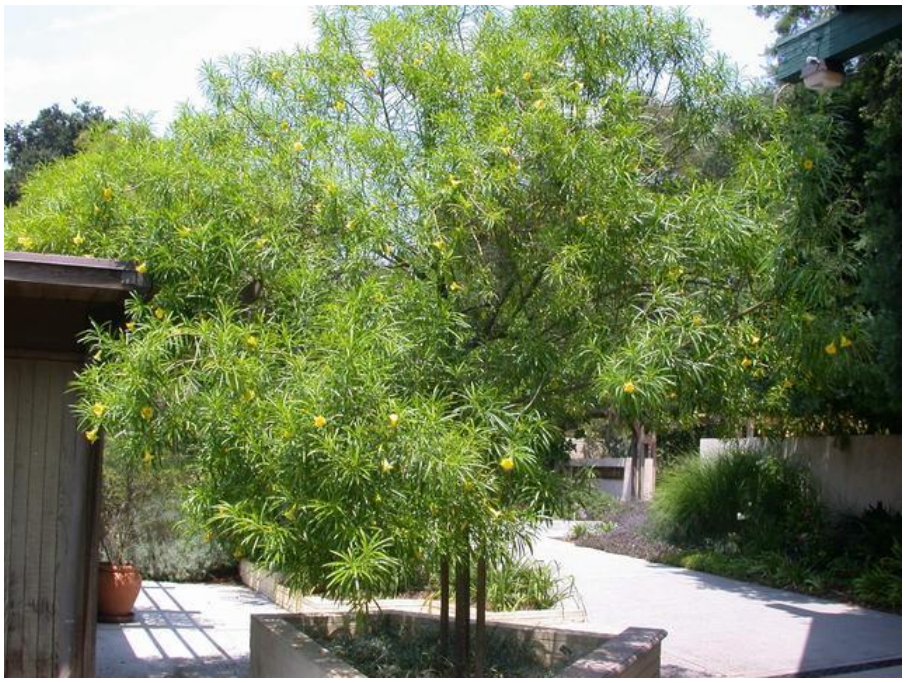
Tab. Orciprenaline - Yes / No

Steroids - Yes / No

Others - Yes / No If yes specify

Outcome: Improved/ Expired / AMA/Absconded / Discharged at request

YELLOW OLEANDER - TREE

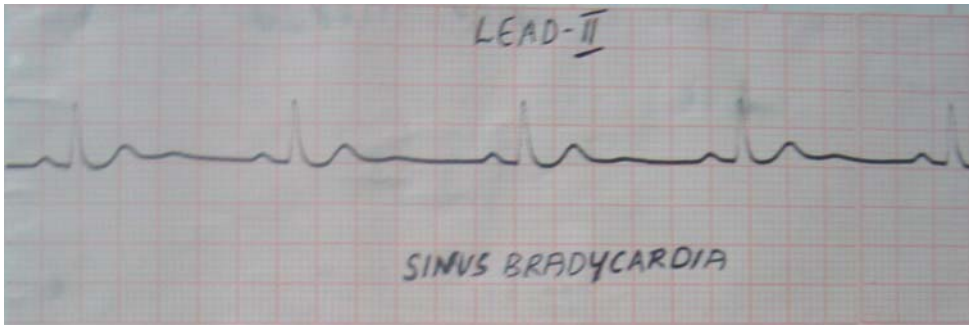


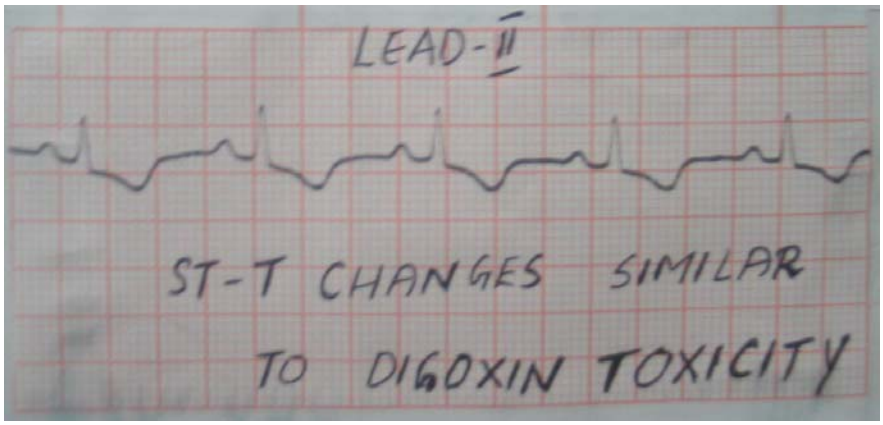
YELLOW OLEANDER – FLOWERS

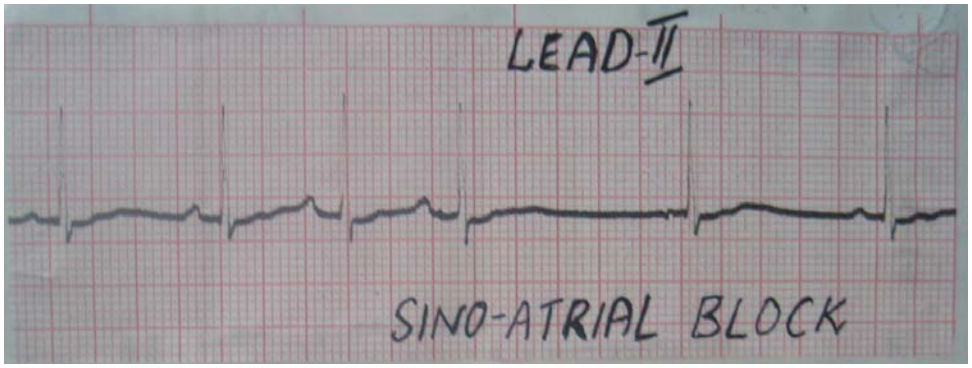
YELLOW OLEANDER - FRUIT

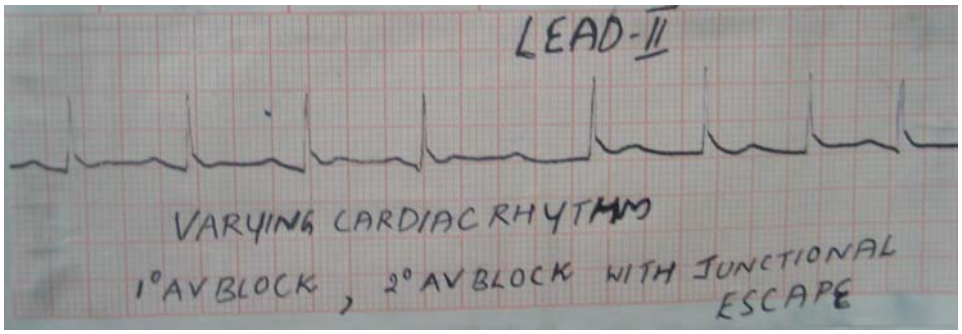
YELLOW OLEANDER – NUT

Selected ECGs of patients of Yellow Oleander poisoning









APPENDIX I

APPROVAL FROM ETHICAL COMMITTEE

Ref.No.21156/Ed/1/05 — Government Rajaji Hospital, Madurai-20. Dt. 12.12.05

Minutes of the Ethical Committee Meeting held on 1.12.05 at 12.30 P.M. at the Chamber of the Dean, Government Rajaji Hospital, Madurai.

...

The following members of the Committee have attended the meeting.

1. Chairman i/c. of Ethical Committee
2. Professor of Surgical Oncology
3. Professor of Medicine
4. The Director, i/c. of Institute of Pharmacology

The members of the Ethical Committee have approved the following Projects.

Name	Project	Remarks
1.Dr.S.Karuthapandian Prof. & H.O.D.of Biotechnology Alagappa University Karaikudi-630 003.	Permission to obtain throat swabs from Paediatrics& E.N.T. Departments	Approved.
2. Prof. & H.O.D. of Medicine, Govt. Rajaji Hospital, Madurai.	Nutrition & Health status of Fisherman	Approved
3. Dr.Vimal Abraham P.G.in M.D.General Medicine Madurai Medl.college Madurai	Socio-Clinical Bio-Chemical &ECG Aspects of Oleander Poisoning	Approved
4. Dr.V.Amin P.G.in M.D.(Gen.Med.) Madurai Medl.College Madurai	Serum Calcium level in newly diagnosed hypertension	Approved
5. The Prof. & H.O.D. of Medicine,O.R.H. Madurai.	Psychological & Phisical Well being and HIV/AIDS	Approved
6. The Prof. & H.O.D. of Medicine O.R.H.Madurai	Health Care Workers and HIV/AIDS	Approved
7. C.Cecilia Xavier Jyothi II Year MBBS., Madurai Medl.College Madurai	Serum Zinc level in Pulmonary Tuberculosis patients	Approved
8. A.V.Nadhkumar Adhitya II year MBBS., Madurai Medl.College Madurai	Noise levels in the Hospital Environment	Approved

-2-

9.	Mullai Veluthambi CBRI., Madurai Medl.College Madurai	ACE Gene Polymorphism in Myocardial Infarction	Approved
10.	Dr.R.Baskaran P.G. in M.D.(Pharm.) Madurai Medl.College Madurai	Prescription from the point of Doctors and Community	Approved

Note: All those are doing project on Research work are instructed to submit a detailed summary of their work to the Ethical Committee on completion of the work.

2. All those who are involved in their workx should duly acknowledge the ethical approval in their work.

3. The Project or Research work should be limited for which the Ethical Committeehas given approval.

4. They should not x violate Ethical Approval and limites/ regulations.

5. If any modofication or not approved, a fresh application will be required.

True copy forwarded

(Sd.) x x x
Dean/Chairman, Ethical Committee
Govt.Rajaji Hos,ital,Madurai.

Administrative Officer.

To

The individuals thro' proper channel.

Copy to: The Ethical Committee Members
Govt.Rajaji Hospital and
Madurai Medical College,Madurai.

mp.

MASTER CHART KEY

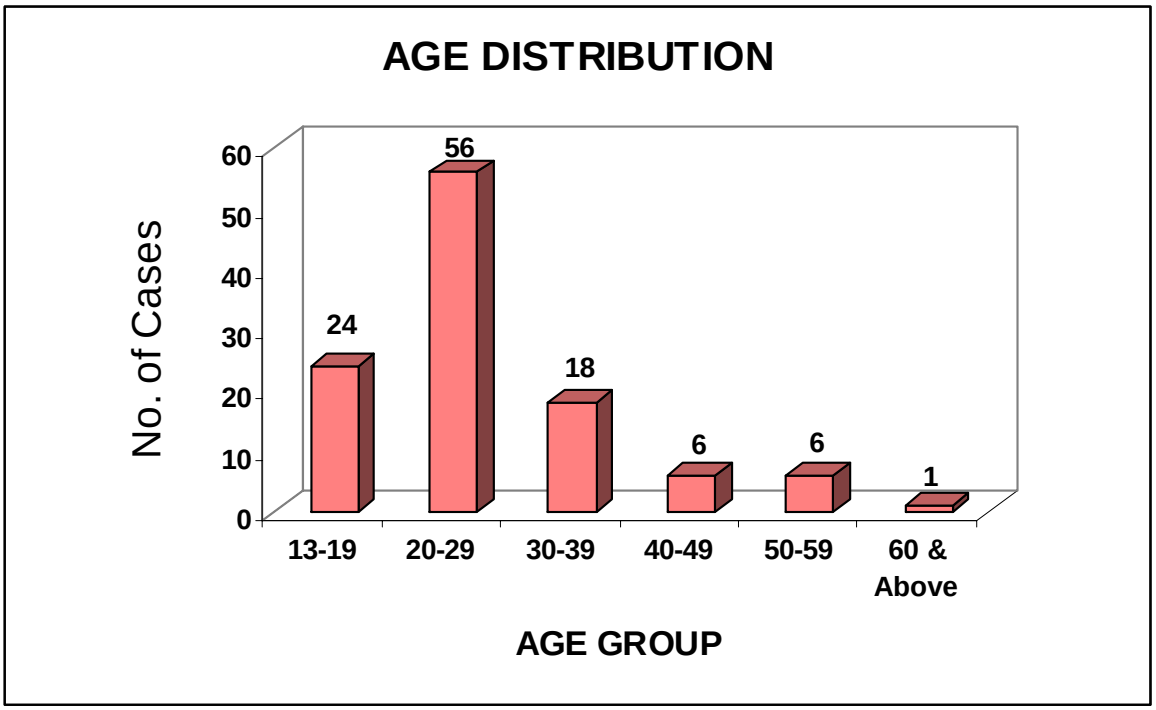
YELLOW OLEANDER POISONING

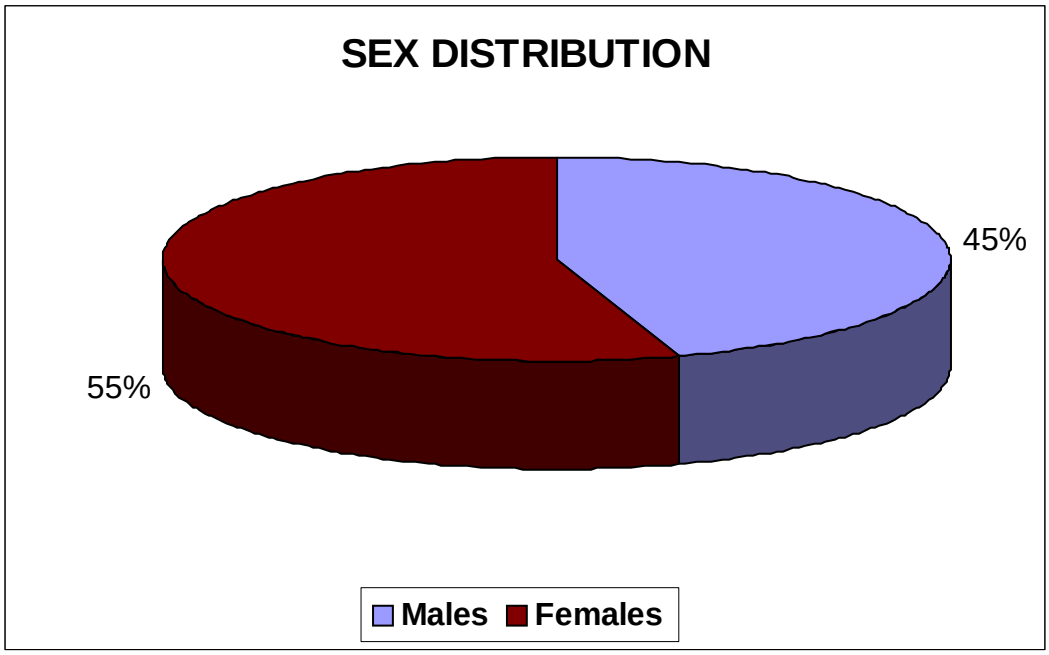
1. Sex	Male – 1	Female – 2	
2. Marital Status	Married - 1 Divorcee – 4 Not recorded – 9	Unmarried – 2 Widow – 5	Separated – 3 Widower – 6
3. Part ingested	Fruit – 1 Leaves – 4	Seed / kernel – 2 Root – 5	Flower – 3 Other parts – 9
4. Method of ingestion	Crushed – 1 Swallowed – 3	Chewed -2 Others – 4	
5. Consumption in	Empty stomach – 1	After Food – 2	
6. Intention	Suicidal – 1 Homicidal – 3	Accidental – 2 Others - 4	
7. First Aid → Given → 1		Not given → 2	

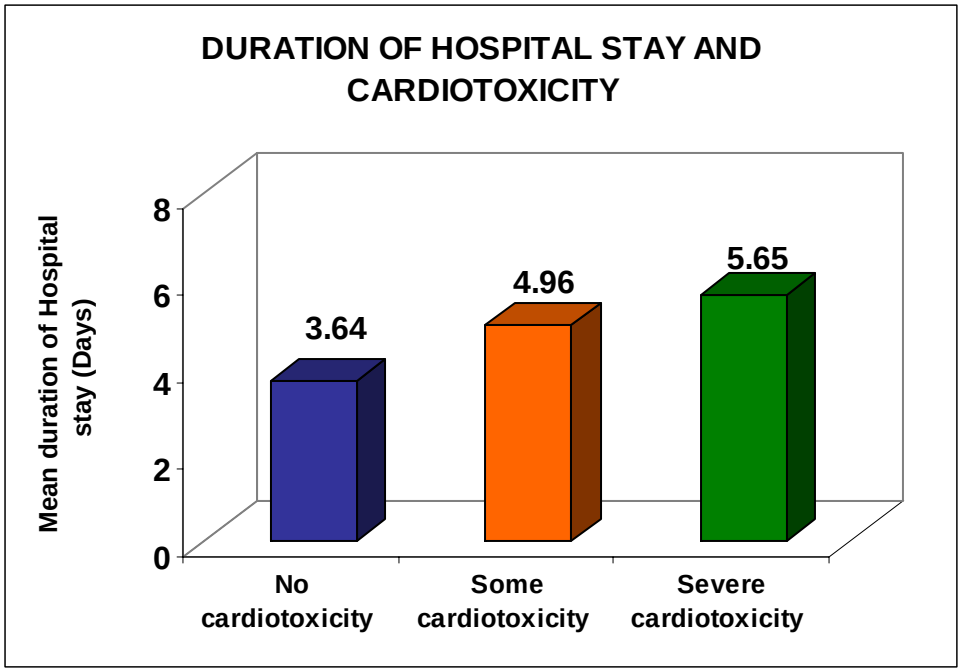
8. Treatment by other doctors	Yes – 1	No – 2
9. Vomiting	Yes – 1	No – 2
10. Abdominal Pain	Yes – 1	No – 2
11. Diarrhea	Yes – 1	No – 2
12. Giddiness	Yes – 1	No – 2
13. Numbness of tongue & lips	Yes – 1	No – 2
14. Altered mental status	Yes – 1	No – 2
15. Blurred vision	Yes – 1	No – 2
16. Palpitations	Yes – 1	No – 2
17. Shortness of breath	Yes – 1	No – 2

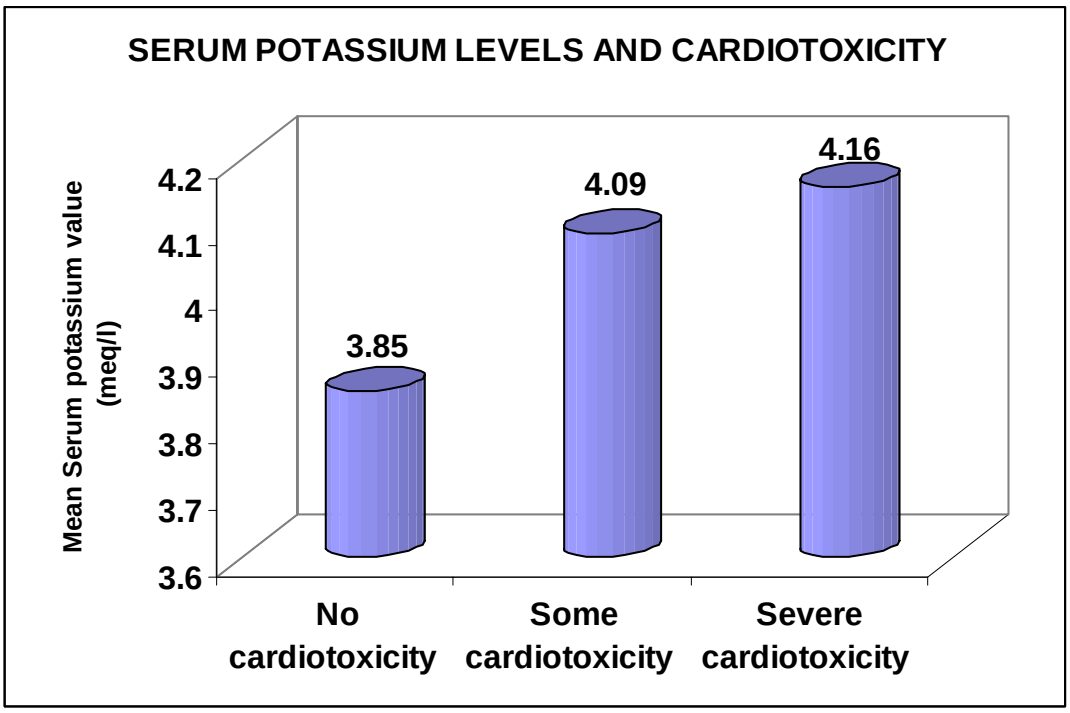
18. Pulse rhythm	Regular -1	Irregular – 2
19. Sinus rhythm	Yes – 1	No – 2
20. Sinus bradycardia	Yes – 1	No – 2
21. Sinus arrestor exit block	Yes – 1	No – 2
22. Atrial Ectopics	Yes – 1	No – 2
23. Junctional rhythm	Yes – 1	No – 2
24. AV Dissociation	Yes – 1	No – 2
25. 1° AV block	Yes – 1	No – 2
26. 2° AV block	Mobitz Type I block – 1 Mobitz Type II block – 3	No block – 2
27. 3° AV block	Yes – 1	No – 2
28. ST – T Changes	Yes – 1	No – 2
29. Gastric lavage	Yes – 1	No – 2
30. Injection Atropine	Yes – 1	No – 2
31. Tablet Orciprenaline	Yes – 1	No – 2
32. Steroids	Yes – 1	No – 2

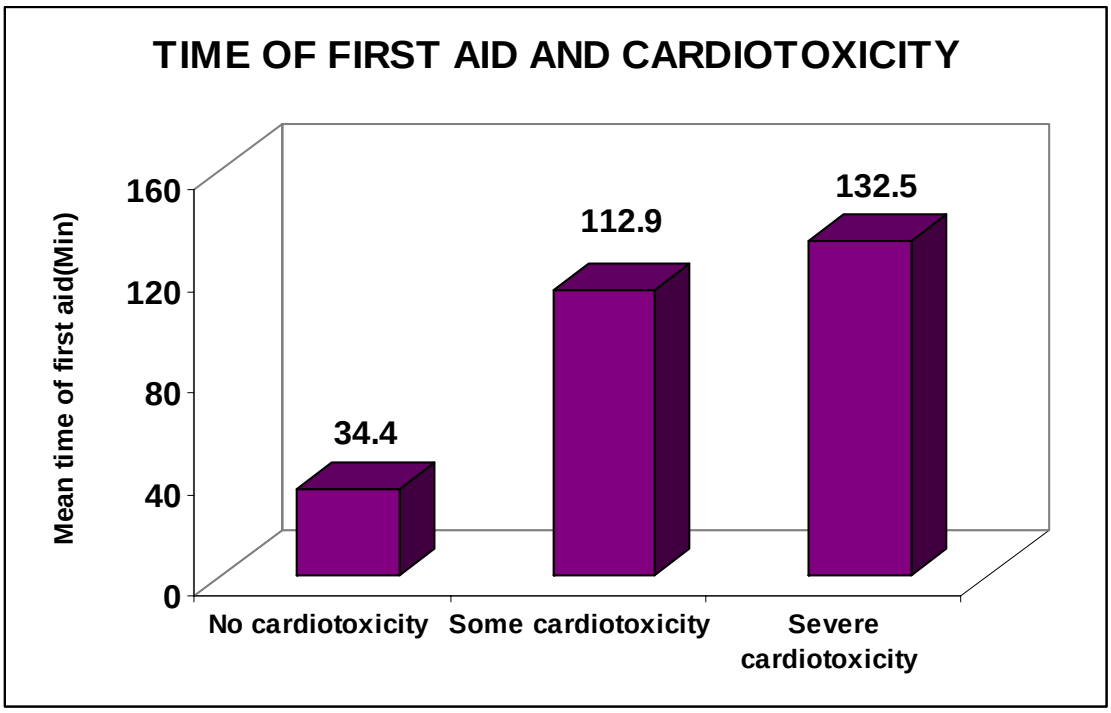
33. Outcome	Improved – 1	Expired – 2
	Against Medical Advice – 3	Absconded – 4

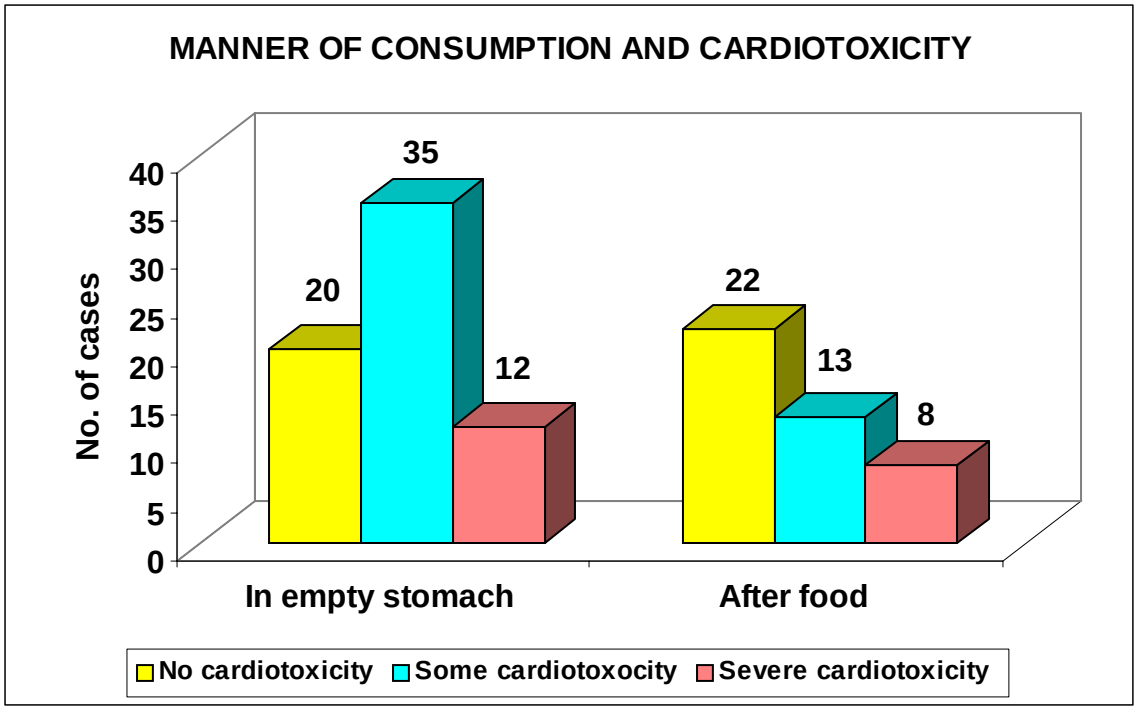

AGE DISTRIBUTION
No. of Cases
60
50
40
30
20
10
0
24
56
18
6
6
1
13-19
20-29
30-39
40-49
50-59
60 & Above
AGE GROUP


SEX DISTRIBUTION
45%
55%
Males
Females

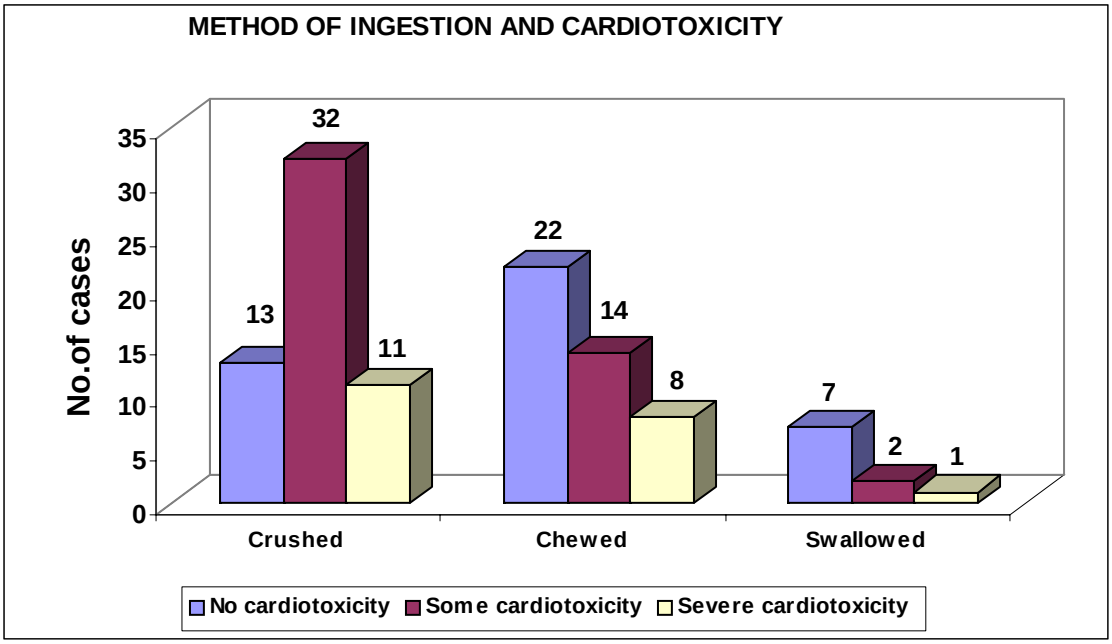

DURATION OF HOSPITAL STAY AND CARDIOTOXICITY
Mean duration of Hospital stay (Days)
0
2
4
6
8
3.64
4.96
5.65
No cardiotoxicity
Some cardiotoxicity
Severe cardiotoxicity

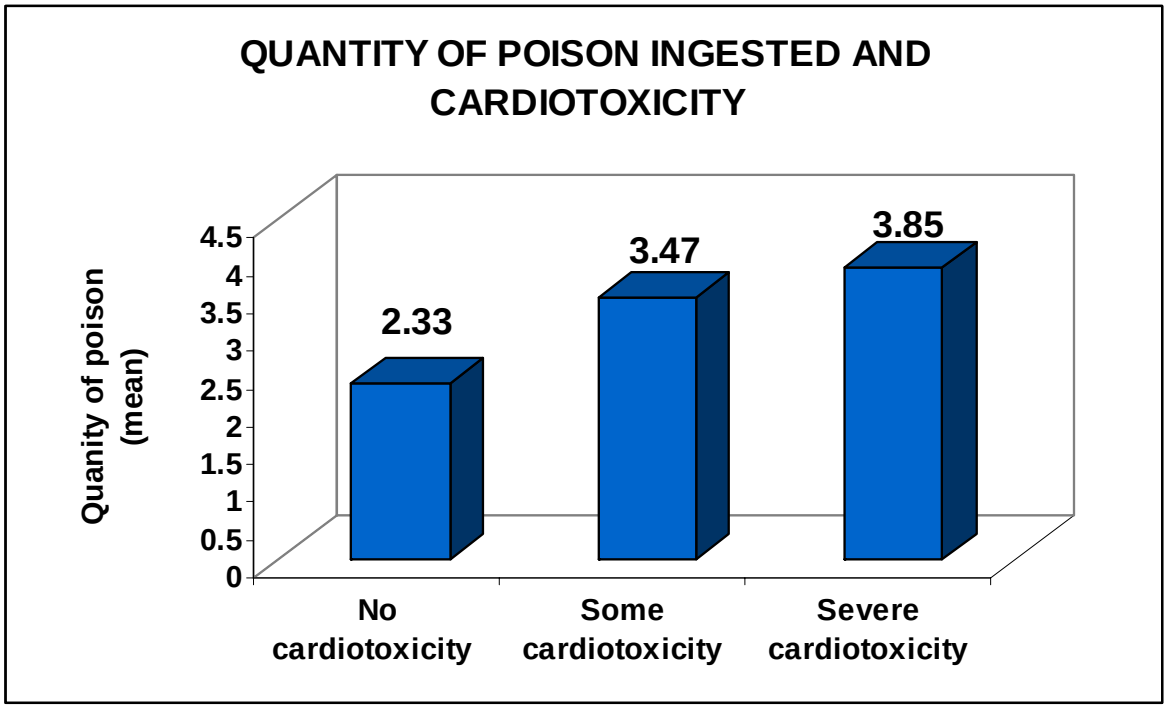

SERUM POTASSIUM LEVELS AND CARDIOTOXICITY
Mean Serum potassium value (meq/l)
4.2
4.1
4
3.9
3.8
3.7
3.6
3.85
4.09
4.16
No cardiotoxicity
Some cardiotoxicity
Severe cardiotoxicity

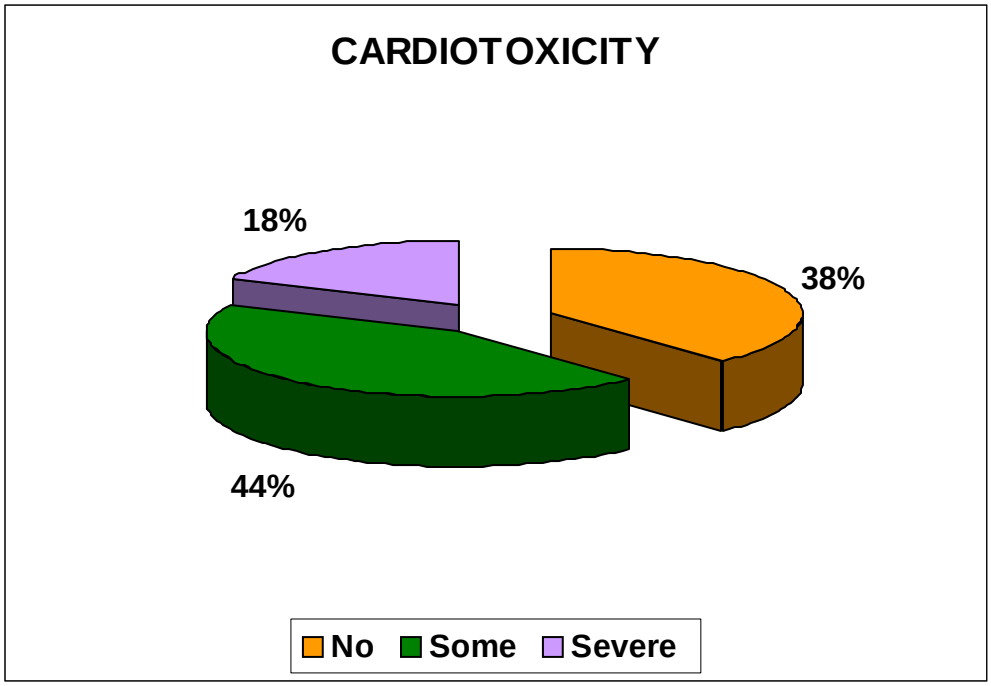

TIME OF FIRST AID AND CARDIOTOXICITY
Mean time of first aid(Min)
160
120
80
40
0
34.4
112.9
132.5
No cardiotoxicity
Some cardiotoxicity
Severe cardiotoxicity


MANNER OF CONSUMPTION AND CARDIOTOXICITY
No. of cases
40
35
30
25
20
15
10
5
0
20
35
12
22
13
8
In empty stomach
After food
No cardiotoxicity
Some cardiotoxocity
Severe cardiotoxicity

]


METHOD OF INGESTION AND CARDIOTOXICITY
No.of cases
35
30
25
20
15
10
5
0
13
32
11
22
14
8
7
2
1
Crushed
Chewed
Swallowed
No cardiotoxicity
Some cardiotoxicity
Severe cardiotoxicity


QUANTITY OF POISON INGESTED AND CARDIOTOXICITY
Quanity of poison (mean)
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
2.33
3.47
3.85
No cardiotoxicity
Some cardiotoxicity
Severe cardiotoxicity


CARDIOTOXICITY
18%
38%
44%
No
Some
Severe